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The Control of Environmental Lung Cancer Hazards
A Critical Appraisal

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Fort Myers, Florida

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The Control of Environmental Lung Cancer Hazards
A Critical Appraisal

W.C.Hueper M.D.
Fort Myers,Fla.

I. General Biologic Principles and Facts

A critical assessment of the merits of present and contemplated control measures suitable for combatting the growing threat of environmental lung cancer hazards to human health must take proper account of the following established biologic principles and basic facts related to pulmonary carcinogenesis.

1. It is a scientifically and legally recognized fact that cancers of the lung can be induced in man upon proper and usually occupational exposure by a variety of chemicals inhaled in the form of dust,fumes, mists,vapors or gases(coal tar,petroleum oils,isopropyl oil,mustard gas, radon and radioactive dust,chromium compounds,nickel,arsenicals,asbestos). Lung Cancers thus have a polyetiology(Hueper,1942,1955,1966;Hueper and Conway,1964).

2. It is to varying degrees less well established that the environmental and occupational inhalation of air contaminated with incomplete combustion and distillation products of various types of carbonaceous materials(coal,petroleum,wood,tobacco,gasoline,diesel oil,soot,etc.), and industrial and agricultural air pollutants(arsenicals,chromates,nickel, iron, radioactive chemicals,asbestos,beryllium) containing human carcinogens.

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3. The observation of a carcinogenic action upon the lungs of experimental animals by several chemicals used in the human economy(ethyl carbamate,several nitrosamines,isoniacid,4-nitroquinoline-N-Oxide) for medicinal,pesticidal and industrial chemical purposes suggests that the existing knowledge of pulmonary human carcinogens is defective. A similar connotation has the fact that some of the recognized human carcinogenic chemicals,originally known only for their action on the skin,where subsequently found to have also a carcinogenic effect upon the lungs(coal tar, petroleum products,arsenicals). It is therefore likely that some of the economically important chemicals which have induced cancerous reactions so far only in non-respiratory organs might have upon proper exposure a carcinogenic action on the human lungs(water soluble and insoluble carbon and silicon polymers,oxidized vegetable and animal fats,chlorinated hydrocarbons,formaldehyde,aliphatic and aromatic epoxides,etc.). Human and experimental observations attest to the pluripotentiality of carcinogens.

4. Experimental evidence proves and human evidence suggests that cancers of the lung may be induced not only when carcinogens are inhaled but also when they are introduced by other,non-respiratory routes(oral,parenteral)(arsenicals,benzidine,nitrosamines,isoniacid,4-nitroquinoline-N-oxide).

5. Since cancers caused by environmental natural or man-made carcinogens can be controlled by appropriate preventive,prophylactic and protective measures,whenever their identity is known and their sources of production,their channels of subsequent dissemination,their pattern of environmental distribution ,the types and the opportunities of exposure to them,and the population groups exposed to them have been established, it follows that environmental lung cancers fulfilling such requirements

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should be amenable to preventive control measures.

6. Because of the distinct complexity of the known part of the respiratory environmental carcinogenic spectrum, it is not feasible to devise at present a lung cancer prevention program which is all inclusive and at the same time equally effective for all members of this spectrum. There are moreover distinct differences in the degree of significance of the lung cancer hazards created by the various recognized and suspected pulmonary carcinogens.. It is therefore necessary to have a well balanced study and control program which avoids carefully any unintentional or intentional miscalculations and exaggerations on this point to insure optimal efficiency and maximal economy for the measures taken . Because of the long latent period of environmental cancers which will continue to appear for some 20 to 30 years after complete cessation of exposure to a carcinogenic agent, the merits or demerits of control measures can be judged properly only some 10 to 15 years after their introduction. Faulty decisions in such matters therefore may be not only a source of disappointment but may have also disastrous results for the populations exposed to pulmonary cancer hazards excluded from or neglected in a program of lung cancer prevention.

Adequate knowledge as to the nature of an environmental lung cancer hazard is especially essential when designing prophylactic and protective measures. The lack of such information can lead to serious failures. The dismal history of lung cancer prevention among the radioactive cobalt ore miners in Schneeberg whose occupational lung cancers were recognized in 1879 long before the discovery of radioactivity provides a striking illustration of such regrettable and avoidable experiences. They are at present particularly appropriate to be remembered because of the evidently defective evidence regarding the causal agents allegedly responsible for the occurrence of lung cancers in cigarette smokers.

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These fundamental biologic principles,facts and observations have obtained during recent decades unusual importance because of the remarkable and progressive increase in the frequency of lung cancer starting around the turn of the century and the growing and assertive clamor emanating from governmental and private sources incriminating cigarette smoking as the predominant cause of cancer of the lung and of a host of diverse additional diseases as well as of their alarming rise in frequency(Terry;Lickint;Graham and Wynder;Wynder;Hammond and Horn;Hammond;Breslow;Levin;Ochsner;Shimkim;Dorn; Haenszel;Delarue;Best et al.;Doll; and many others). Lung cancers represent, according to this newly developed theoretical concept of "cigarette diseases", a group of highly divergent disorders which have become increasingly frequent during the last few decades and which allegedly are all caused by or associated with cigarette smoking(cancers of the lung,larynx,oral cavity,esophagus, & bladder; chronic bronchitis,emphysema,arteriosclerosis,coronary sclerosis, thromboangiitis obliterans,gastric ulcer). This concept attributes to tobacco smoking disease producing properties which in their diffuseness and vagueness carry an almost embarrassing resemblance to the long abandoned belief in "miasmatic diseases". Tobacco smoke has become,according to such claims,the most important single cause of disease,disability and death in recent years. High officials of the U.S.Public Health Service professed that cigarette smoking had been responsible in 1967 for about 300,000 excess deaths in the United States or for nearly as many deaths as those due to all types of infections, all accidents,suicides,murders,and diabetes combined(Wm.Stewart).

According to the bold claims of many proponents of the cigarette theory of lung cancer,it is held that the great majority of these cancers (80 to 90 per cent) are attributable to cigarette smoking,that therefore most of the 50,000 deaths from this cancer recorded in 1967 in U.S.A. would

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have been preventable,and that the problem of the causation of this cancer had satisfactorily been solved and that therefore no further research into the causes of this cancer were needed(Wm.Stewart).

If such astounding declamations by public health officials would be accepted at face value,it would appear that further badly needed investigations into the etiology of lung cancer would be relegated to a position of minor importance in cancer research and public health practice through allotting greatly reduced funds,facilities,personnel,and prestige to such studies, dealing with the important role of the various non-tobacco factors of well established etiologic significance. At the same time the bulk of all efforts at lung cancer control would center around measures aimed at reducing the cigarette smoking habit or at making cigarette smoking safe while neglecting the equally,if not more important,control of the various lung cancer hazards of non-tobacco origin related to atmospheric pollutants and occupational factors. Such a development is definitely unsound for scientific reasons and is definitely not in the public interest quite apart from the fact that it represents objectionable public health practice,as evident from the following analysis of the various observations and arguments advanced in support of the cigarette theory of pulmonary carcinogenesis.

For the purpose of this discussion the following observations and their interpretations are accepted as facts or near-facts:

a. There can be no reasonable doubt that the remarkable increase in the frequency of lung cancers observed in many countries during the past 70 years has been real to a large extent,although an increased awareness of the medical profession as to the occurrence of lung cancers,improved diagnostic methdds,better biostatistical recording,and a growing use of post mortem examinations assume a certain share in accounting for this phenomenon.

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Since the observed upward movement of lung cancers as a cause of death started around the turn of the century, it can be assumed that some 20 years earlier ,corresponding to the average length of the latent period of environmental and occupational cancers,either previously present carcinogens became more active or new carcinogens were introduced into the human environment or both developments occurred simultaneously. Because of the marked variations in the time of onset in the rise of lung cancers in the total cancer panorama noted for different countries,regions,and communities this irregular epidemiologic pattern in the quantitative and qualitative local action of respiratory carcinogens represents an additional etiologically important facet of the increasing frequency of lung cancer,especially since similar local differences have been noted in the sex distribution as well as in the ratio of different histologic types of cancers of the lung. A striking lack in uniformity of various aspects characterizes the observed rise in the occurrence of lung cancers. This phenomenon deserves adequate consideration in determining the scientific merits of the cigarette theory of pulmonary carcinogenesis.

b. The consumption of cigarettes,like that of many other items of daily living,has increased considerably and progressively during the last 70 years,especially since World War I,in most countries,but again this growth in the cigarette smoking habit has exhibited marked variations in different countries and in different population groups and between members of the two sexes.

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c. Reliable chemical analyses have demonstrated definitely that cigarette smoke contains several different carcinogenic chemicals,such as especially several nown polycyclic aromatic hydrocarbons,of which 3,4-benzpyrene is the prototype,as well as arsenic,nickel,selenium,polonium,and probably nitrosamines. All of them are present in rather minute amounts.

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The principal arguments and the most important evidence advanced in support of the cigarette theory of lung cancer cover the following points:

a. The rise in frequency of lung cancer followed by about 15 to 20 years the growth in the consumption of cigarettes, and ran roughly parallel to it.

b. This relation was not merely coincidental but reflected a causal asspciation because the degree of liability to develop lung cancer by an individual increased with his daily numerical consumption of cigarettes.

c. The preponderance of males to develop lung cancer was the result of their higher consumption of cigarettes and their longer indulgence in this habit when compared with females.

d. The high statistical association of cigarette smoking to lung cancer indicated that general air pollutants and occupational atmospheric carcinogens played a minor role in the causation of lung cancers, if any.

e. The reported increase in the squamous cell type of lung carcinoma was etiologically related to cigarette smoke introduced into the respiratory ducts and thus provided additional proof of the alleged cigarette causation of such cancers.

f. The more common consumption of cigarettes by the urban populations than by rural ones accounted for the greater frequency of lung cancer in urban areas.

Although it may be conceded that the mainly statistical evidence underlying these theses lends on superficial examination a certain support to the theory of the cigarette causation of lung cancers, this conclusion becomes readily uncertain, if not unacceptable, if critically studied in the light of the many contradictory observations inconsistent with the above precept.

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II. Critical Assessment of Methods, Criteria and Evidence

A balanced, rational and competent judgement concerning the relative scientific merits of the methods, criteria and evidence used in support of the cigarette theory requires that they be examined in the light of the total information available on these aspects for other, non-tobacco factors incriminated in pulmonary carcinogenesis as well as for environmental carcinogens and cancers in general.

A. Epidemiologic Pattern of Lung Cancers

The epidemiologic pattern of lung cancers exhibits numerous features which are inconsistent with the cigarette theory, or permit more probable or more plausible explanations or which have been subjected to distorted or inadequate or fallacious explanations so as to be in harmony with this theory.

1. Time of Onset and Geographical Distribution of Observations on Increase of Lung Cancers

The advocates of the cigarette theory have claimed that the increase in lung cancer throughout the world followed upon the rapid and marked growth of the cigarette smoking habit which occurred especially during and after World War I.

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Published records show that a real, definite and progressive increase in the frequency of lung cancers started in many industrialized countries around the turn of the century, when the cigarette smoking habit was still of minor significance (Probst; Berblinger; Grosse; Kahlau; Fischer; Hueper). Table 1 However, this was not a uniform development, but affected first only circumscribed areas or communities (Hueper, 1942; 1926; 1955; 1965), leaving others unchanged. In Germany an increase of lung cancers was first noted in Saxony, especially in two industrialized cities, and Central Germany only, while such changes were absent

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Table 1. Frequency rates of lung cancers in autopsy material (Probst)

Author	Period	Number of autopsies	Total carcinomas	Absolute No.	Lung cancers	
					Percent of all cases	Percent of all autopsies
	1852–1900					
Reinhard	1852–76	8, 716		5		0. 057
Fuchs	1854–85	12, 307		8		. 065
Wolf	1877–84	4, 172		9		. 21
Passler	1881–94	9, 246	870	16	1. 83	. 17
Wolf	1885–94	7, 228		31		. 428
Perutz	1885–97			9	1. 27	. 10
Marchesani	1887–96	1, 946		4		. 26
Kikuth	1889–99			10		. 07
Feilchenfeld	1895–1900	5, 022	511	22	4. 3	. 24
Riechelmann	1895–1901	7, 790	711	27	3. 8	. 39
Sehrt	1899–1903	1, 741	159	3	1. 88	. 17
Marchesani	1886–1906	3, 337		6		. 18
	1900–1925					
Redlich	1900–05	2, 002	496	31	6. 3	1. 5
Seyfahrt	1900–06				5. 1	. 67
Karrenstein	1900–07	10, 272	934	32	3. 42	. 31
Kikuth	1900–11			90	3. 8	. 37
Staehelin	1900–11		566	12	2. 1	
Bejach	1904–08		715	20	2. 79	
Probst	1906–10	2, 739	265	3	1. 13	. 11
Seyfahrt	1907–13				6. 88	. 9
Briese	1898–1916	12, 971	1, 287	60	4. 51	. 46
Bejach	1908–13	6, 808	692	33	4. 8	. 45
Bejach	1909–12	5, 801	586	29	4. 95	. 5
Marchesani	1906–16	4, 754		6		. 13
Rau	1909–14	4, 816	552	15	2. 7	. 31
Berblinger	1910–14	2, 347	363	8	2. 2	. 34
Materna	1912–14	866	48	1	2. 08	. 11
Staehelin	1912–14		218	11	5. 0	
Probst	1911–15	3, 448	389	13	3. 34	. 38
Seyfahrt	1914–18				11. 23	1. 01
Assmann	1912–22					. 19
Materna	1915–17	1, 667	70	5	7. 14	. 35
Breckwoldt	1914–19	6, 083	554	21	3. 7	. 36
Rau	1915–19	5, 518	580	27	4. 8	. 49
Berblinger	1915–19	3, 280	337	10	2. 9	. 30
Probst	1916–20	4, 989	392	24	6. 12	. 59
Materna	1918–20	1, 609	94	5	5. 31	. 31
Kikuth	1912–23			146	5. 8	. 58
Marchesani	1916–22	3, 336		10		. 3
Staehelin	1915–23		755	38	4. 9	
Lubarsch	1920–21		8, 301	458	5. 4	
Seyfahrt	1919–23				8. 75	
Berblinger	1920–24	2, 429	287	24	8. 3	. 99
Materna	1921–23	1, 049	75	6	8. 0	. 57
Breckwoldt	1920–25	6, 359	892	26	2. 7	. 39
Probst	1921–25	3, 697	502	36	7. 17	. 97
Stachelin	1924	749		5	4. 9	

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					Percent of all cases	Percent of all autopsies
	1852–1900					
Reinhard	1852–76	8,716		5		0.057
Fuchs	1854–85	12,307		8		.065
Wolf	1877–84	4,172		9		.21
Passler	1881–94	9,246	870	16	1.83	.17
Wolf	1885–94	7,228		31		.428
Perutz	1885–97			9	1.27	.10
Marchesani	1887–96	1,946		4		.26
Kikuth	1889–99			10		.07
Feilchenfeld	1895–1900	5,022	511	22	4.3	.24
Riechelmann	1895–1901	7,790	711	27	3.8	.39
Sehrt	1899–1903	1,741	159	3	1.88	.17
Marchesani	1886–1906	3,337		6		.18
	1900–1925					
Redlich	1900–05	2,002	496	31	6.3	1.5
Seyfahrt	1900–06				5.1	.67
Karrenstein	1900–07	10,272	934	32	3.42	.31
Kikuth	1900–11			90	3.8	.37
Staehelin	1900–11		566	12	2.1	
Bejach	1904–08		715	20	2.79	
Probst	1906–10	2,739	265	3	1.13	.11
Seyfahrt	1907–13				6.88	.9
Briese	1898–1916	12,971	1,287	60	4.51	.46
Bejach	1908–13	6,808	692	33	4.8	.45
Bejach	1909–12	5,801	586	29	4.95	.5
Marchesani	1906–16	4,754		6		.13
Rau	1909–14	4,816	552	15	2.7	.31
Berblinger	1910–14	2,347	363	8	2.2	.34
Materna	1912–14	866	48	1	2.08	.11
Staehelin	1912–14		218	11	5.0	
Probst	1911–15	3,448	389	13	3.34	.38
Seyfahrt	1914–18				11.23	1.01
Assmann	1912–22					.19
Materna	1915–17	1,667	70	5	7.14	.35
Breckwoldt	1914–19	6,083	554	21	3.7	.36
Rau	1915–19	5,518	580	27	4.8	.49
Berblinger	1915–19	3,280	337	10	2.9	.30
Probst	1916–20	4,989	392	24	6.12	.59
Materna	1918–20	1,609	94	5	5.31	.31
Kikuth	1912–23			146	5.8	.58
Marchesani	1916–22	3,336		10		.3
Staehelin	1915–23		755	38	4.9	
Lubarsch	1920–21		8,301	458	5.4	
Seyfahrt	1919–23				8.75	
Berblinger	1920–24	2,429	287	24	8.3	.99
Materna	1921–23	1,049	75	6	8.0	.57
Breckwoldt	1920–25	6,359	892	26	2.7	.39
Probst	1921–25	3,697	502	36	7.17	.97
Staehelin	1924	749		5	4.9	

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Table 2. Frequency rates of lung cancers in autopsy material of German pathological institutes, 1906–52 [1]

Author	City	Period	Percentage of lung cancers among all cancers	Sex	
				Male	Female
Fischer-Wasels	Frankfurt	1906		1. 6	0. 97
Simross	Goettingen	1906–12	2. 59		
Schairer and Schoeniger.	Jena	1910–14	2. 2		
Peters	Berlin	1913–17	6. 2		
Koch	Dusseldorf	1920–23	3. 61		
Gerbe	Zwickau	1924–27	12. 9		
Buschbek	Dresden	1924–31	19. 79		
Dormanns	Germany	1925–33	13. 0		
Simross	Goettingen	1927–31	9. 83		
Peters	Berlin	1927–31	15. 4		
Gerbe	Zwickau	1928–31	13. 0		
Koch	Duesseldorf	1931–40	12. 28		
Weber and Knoll	Frankfurt	1932	13. 9		
Schairer and Schoeniger.	Jena	1932–39	12. 0		
Fischer-Wasels	Frankfurt	1938		12. 94	2. 38
Koch	Duesseldorf	1942–45	21. 86		
Knorr	Leipzig	1945–48	13. 0		
Emminger and Einfalt.	Bavaria	1945–48		21. 4	4. 8
Koch	Duesseldorf	1946–47	26. 23		
Fischer	Jena	1946–48	13. 0		
Koch	Duesseldorf	1948	35. 53		
Weber and Knoll	Frankfurt	1951	28. 6		
Kahlau	Germany	1952		23. 4	5. 4

[1] From Kahlau.

Fig. 1 Malignant Neoplasm of Lung and Bronchus, and Trachea 1956–57
(M. Segi)

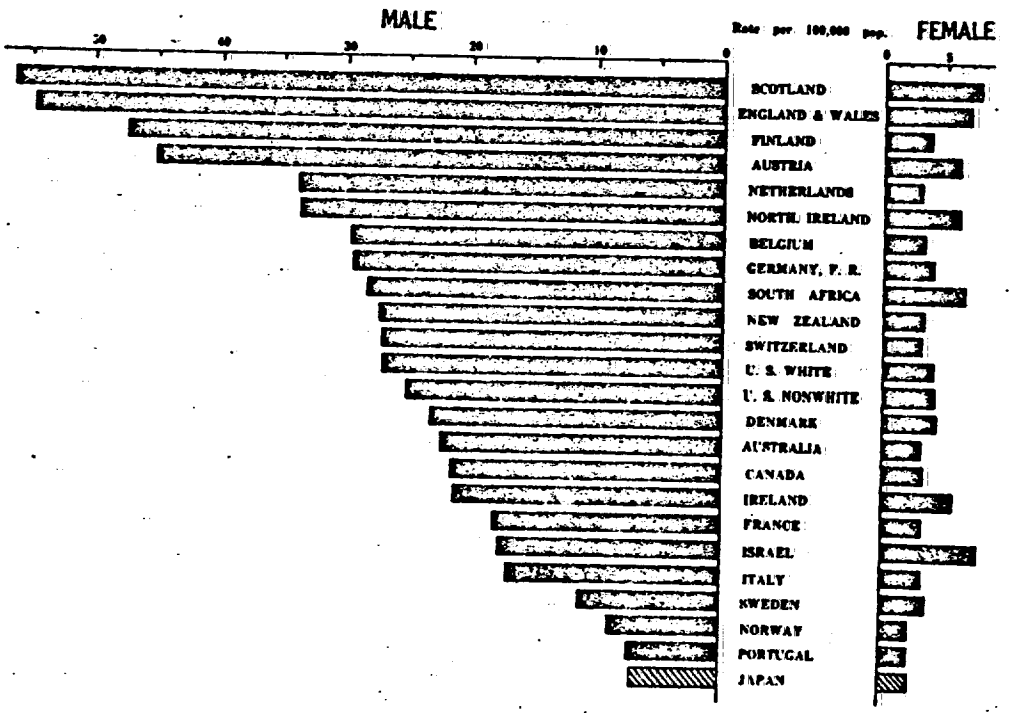

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Table 3.—Annual age-adjusted increase of frequency of lung cancer mortality

Sex	Percent increase		
	1914–30 [1]	1931–40 [1]	1933–44 [2]
Males	10.5	8.5	5.8
Females	8.0	2.5	2.0

[1] Dorn.
[2] Potter.

Figure 2

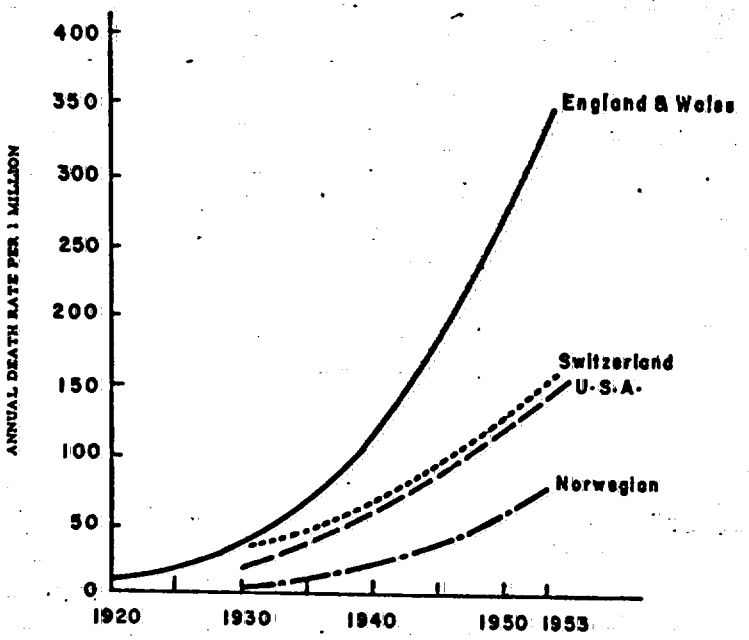

Fig. 1.—Lung cancer death rate rise in several countries (Doll).

TABLE 4.—*Frequency of Deaths from Lung Cancer in Different Countries: Rates per 100,000 Females (P. Kotin)*

Country	Year and Death Rates of Lung Cancers								Position	
	Year	Rate	Year	Rate	Year	Rate	Year	Rate	1952	1930
England & Wales	1930-32	4.3	1949	9.8	1952	11.3	1953	11.8	1	2
Scotland		5.6		10.8		10.9			2	1
Finland	1936-38	2.3		5.4		6.5		5.3	4	6
Switzerland	1929-31	2.0		4.7		4.7		5.4	10	9
New Zealand	1930-32	2.5		3.9		5.1			9	4
Netherlands	1929-31	2.2		4.4		4.0		4.8	12	8
Germany								6.3		
France				5.6		6.1			6	
United States	1929-31	1.9		4.9		5.4		5.11	7	11
Denmark	1934-36	2.5		4.3		6.2		4.8	5	5
Ireland	1935-37	3.2		4.5		7.3			3	3
Australia	1932-34	2.3		3.6		4.3			12	7
Canada	1930-32	2.0		4.6		4.0			14	10
Italy	1931	1.4		3.4		4.5		9.0		
Norway	1929-31	1.2		3.6		5.4			8	13
Japan				1.2		2.2			15	
Israel								10.8		

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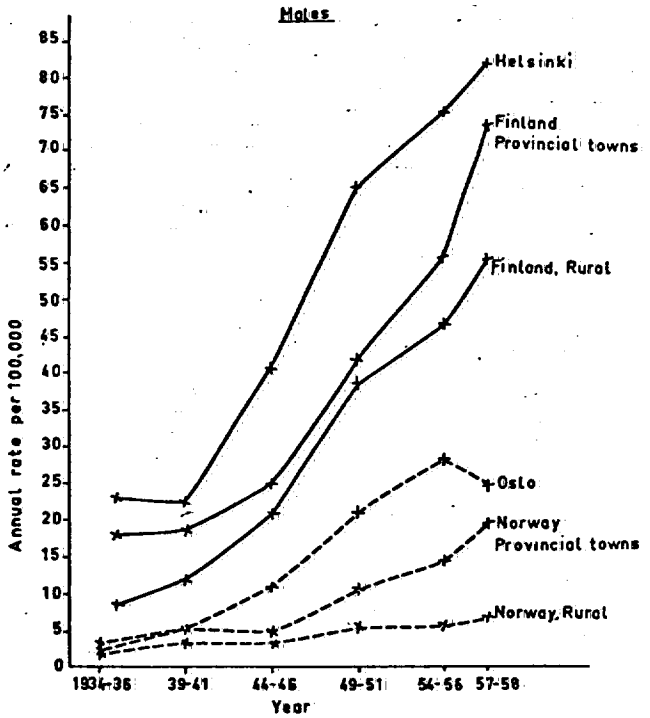

FIG. 5a.—Mortality from lung cancer in Finland and Norway, 1934–58, by residence. Annual age-adjusted rates per 100,000. (Calculated as for Fig. 4.)

4a

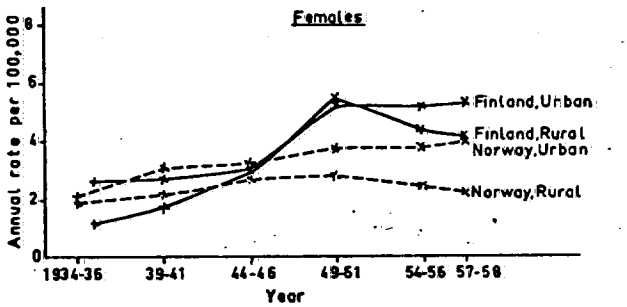

FIG. 5b.—Mortality from lung cancer in Finland and Norway, 1934–58, by residence. Annual age-adjusted rates per 100,000. (Calculated as for Fig. 4.)

4b

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Of distinctly greater significance are the observations of Dorn on the behaviour of the annual age-adjusted progression rate of lung cancer mortality. He found that it was between 1913-1930 for males 10.5, for females 8.0; between 1931-1940 it was 8.5 and 2.5, respectively, and between 1933-1948 it had dropped to 5.8 and 2.0, respectively. Table 3 In a recent report on the experiences in Canada on this point, Phillips stated that the cohort analyses revealed a much slower increase in the rate of rise of lung cancer in generations born after 1906 than in those born before this year. He predicted that the actual death rate would rise more and more slowly in the future.

It is difficult, if not impossible, to reconcile the irregular and, in part contrary, behaviour pattern of progression rates of lung cancers with the concept that an increasing consumption of cigarettes and is proportional to progressively rising lung cancer hazards. These findings again suggest that other, non-tobacco factors contaminating the human environment seem to play a more significant role in this respect, i.e. air pollutants and occupational carcinogens.

c) Urban-Rural Lung Cancer Rates -Geographic Irregularities

The striking and consistent differences in lung cancer rates for inhabitants of metropolitan areas, towns, and rural regions belong fundamentally to the same category of epidemiologic irregularities which have been demonstrated by the widely fluctuating lung cancer rates found in different countries, subdivisions of countries, communities, and subdivisions of metropolitan areas. They all are the result of quantitative and qualitative differences in the composition of the environmental carcinogenic spectrum composed of factors related to various human activities, many known and some evidently still unknown.

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or mild during the first 20 to 30 years of this century in Berlin, Hamburg, Koelln, Basel, and Innsbruck (Table 2). Similar observations concerning a lack of a rise in lung cancer frequency were reported from other countries (England: Bonser; Passey and Holms; Sweden: Ask-Upmark; Denmark: Clemmesen). Even after this development had become more generalized during the last 20-30 years, there remained marked differences in the lung cancer mortality rates between various countries, suggesting that marked quantitative and qualitative variations must exist in the activity of the causative environmental factors (Segi; Phillips; Hueper; Kotin; Pascua; Dunn) (Fig. 1). The operation of such a mechanism is indicated moreover by the fact that distinct discrepancies in the progression rates of the lung cancer increase were observed for different countries (Fig. 2, 3, Table 3, 4; Hueper, 1955; Phillips; Sellers).

A similar connotation have the remarkable differences in lung cancer death rates recorded for various subdivisions (states, provinces, counties, cities, and different parts of metropolitan areas) in individual countries (United States; England; Belgium; Denmark; Japan; U.S.S.R.; Austria) (Lew; Dorn; Mancuso; Patno; Stocks; Hoffman and Gilliam; Prindle; Kennaway and Kennaway; Firket; Herlich and Neubold; Wilder; Segi; Fershtudt; Clemmesen). Commenting on such discrepancies several investigators noted that the high lung cancer rates prevailed in highly urbanized and industrialized regions of the country (Segi; Mancuso; Wilder; Stocks; Firket; Hueper (1955); Doll). The potential etiologic significance of such fluctuations is demonstrated especially by the distinct gradients from high to low lung cancer rates found for central parts of metropolitan districts, their suburban areas and the surrounding rural districts (Prindle; Firket; Stocks) (American cities, London, Liège).

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Identical differences in lung cancer mortality rates have been obtained when such rates were determined for urban and rural regions of various countries (England; North Ireland; United States; Canada; Austria; Norway; France; Switzerland; Italy; Czechoslovakia; Bulgaria; Germany; Finland; Denmark) (Doll; Stocks; Deeg; Howe; Curwen, Kennaway; and Kennaway; Kennaway; Hillis and Cameron; Kennaway and Kennaway; Mancuso; Griswold; Wilder; Gilmore and Anderson; Buell and Dunn; Kotin;

Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Hueper(1966);Gsell and Jung;Gernez-Rieux and Voisin; Gsell;Giovarnardi,Grosso and De Fraja-Frangipana; Saxen and Hakama;Holan and Hudakova;Ancev and Popov; Poche,Mittmann and Kneller;Korpela and Magnus;Clemmesen,Nielsen and Jensen; Oettel;Pedersen;Pedersen and Magnus;Denk;Sellers;Versluys and Meinsma). While many of the investigators cited do not comment on the possible causes of these differences,others concede a major to minor influence of carcinogenic air pollutants in addition to variations in the cigarette smoking habits between rural and urban populations as a significant etiologic factor. A few of the fundamentalists among the advocates of the cigarette theory,however,insist that local differences in the number of cigarette smokers and in the amounts of cigarette consumed solely account for such variations(Kreyberg;Gsell; Oettel). Clemmesen noted that the higher incidence rates for bronchial carcinoma among men in large cities do not justify the assumption of causative factors in town air. He proposed that the 10 year delay in the rise of lung cancers in rural areas of Denmark compared with that in Copenhagen accounts for the differences between urban and rural lung cancer rates and is attributable to a later onset of carcinogenic influences,namely cigarette smoking,in rural habitations than in large conurbations.

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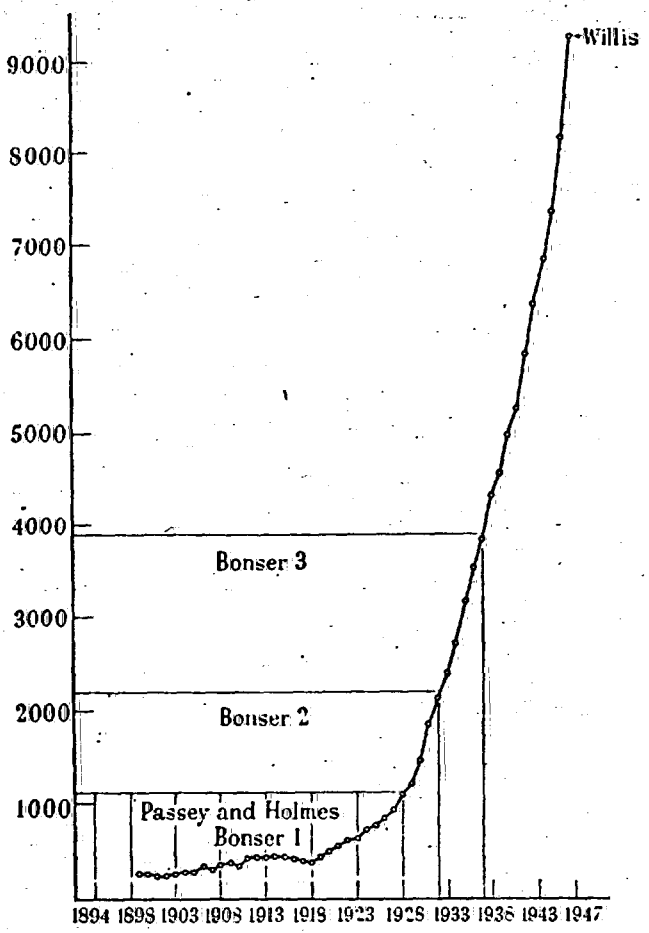
2. Commentary and Appraisal:

a) Time of Onset: Although it must be admitted that the variations in the time of onset of the increase in lung cancers in different regions are in part the result of local discrepancies in the proper recognition of this phenomenon,there remains nevertheless substantial evidence indicating that such fluctuations are real in a significant number of observations,since many of them were made at a time when the medical profession had sufficiently been alerted to this phenomenon,i.e. up to and after 1930. Since the start of this development preceded the widespread adoption of the cigarette smoking

Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000



Heady and Kennaway

FIG. 5.—Cancer of lung. Death certificates. England and Wales, 1899–1947.

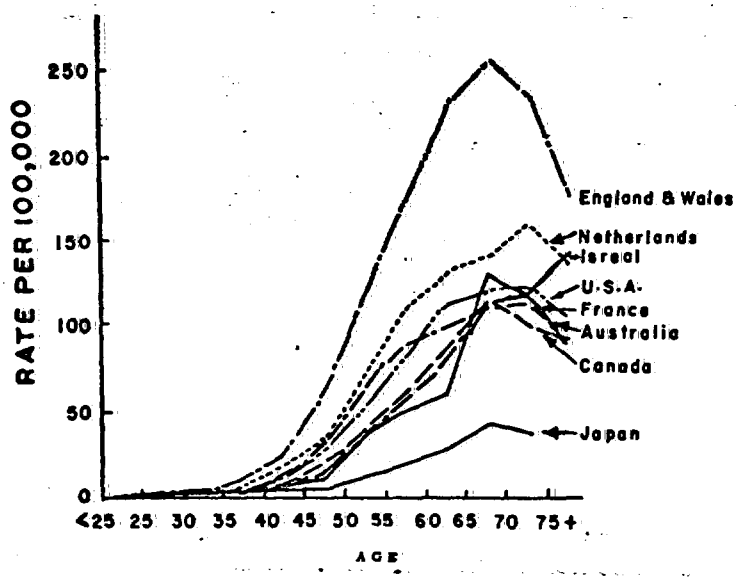


Fig. 6.—Age distribution of lung cancers in different countries (Phillips).

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Fig.A

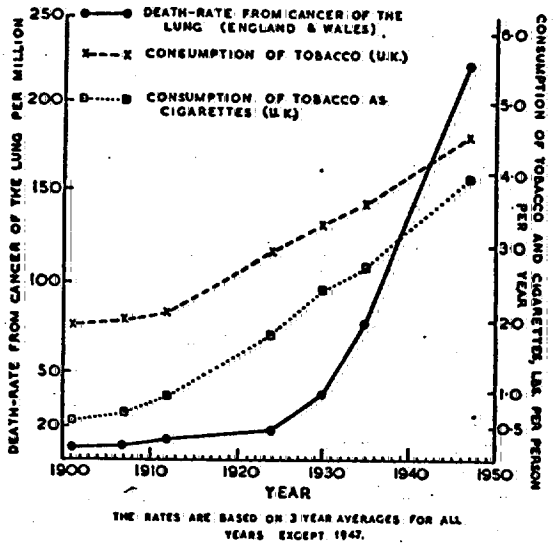

Fig. 6. — Death rate from Cancer of the Lung and Rate of Consumption of Tobacco and Cigarettes.

R.Doll

Fig.B

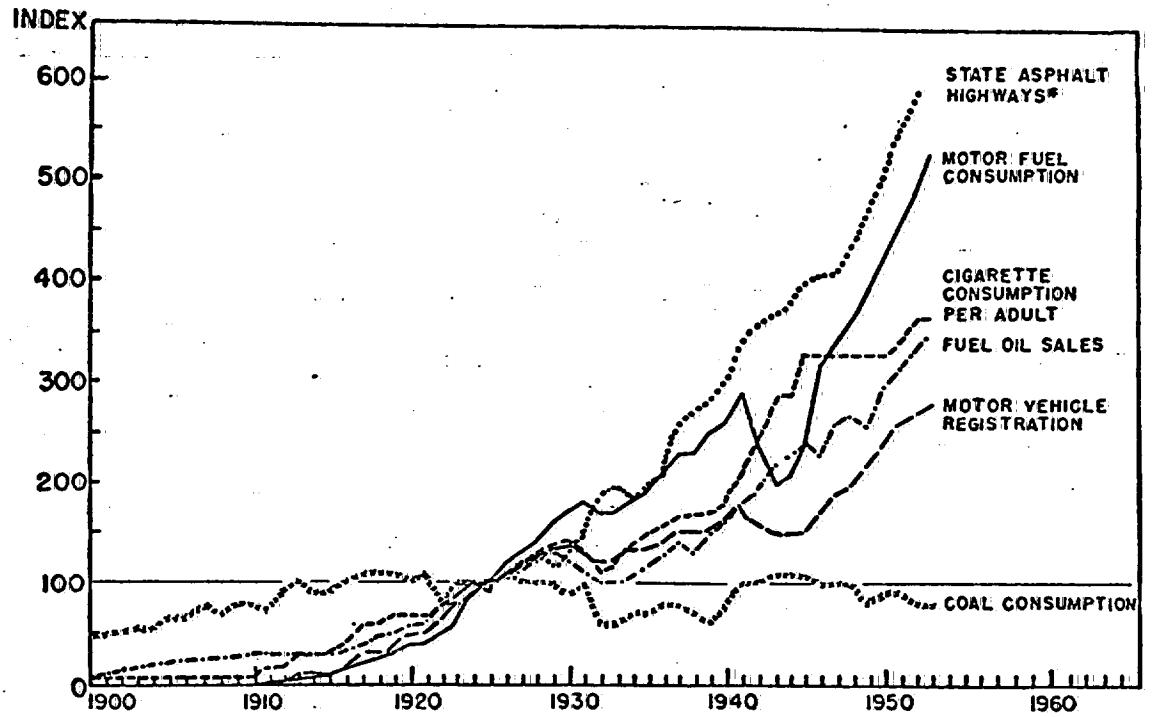

CHART 8.—Trends in selected environmental factors, U.S., 1900–1953 (1924–28 = 100). Note: Cigarette consumption per adult reflects entire population rather than that segment which smokes. Data obtained through courtesy of Dr. E. C. Hammond.

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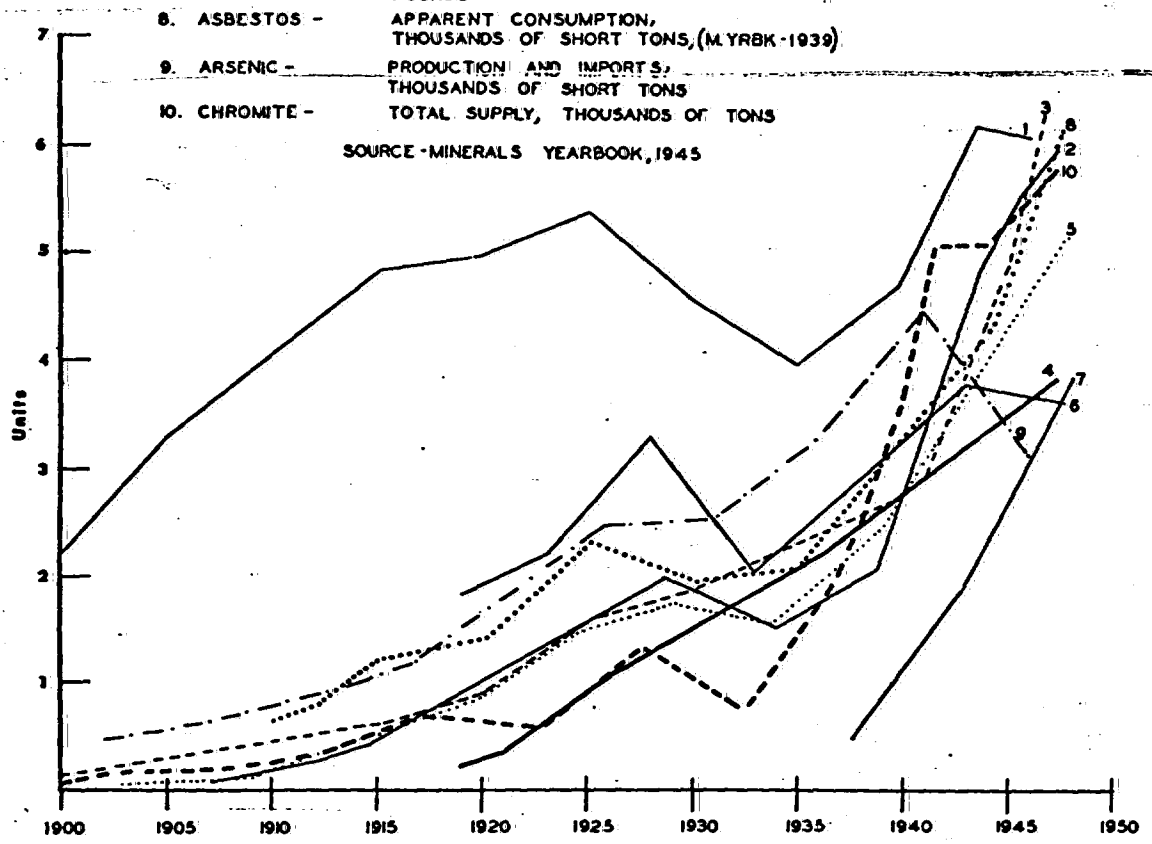
Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Fig.C

Figure 7. Rise in annual production or consumption of cancer-related industrial chemicals between 1900 and 1948.

	PRODUCT	UNIT
1.	BITUMINUS COAL	PRODUCTION IN U.S., MILLIONS OF NET TONS
2.	FUEL BRIQUETS	TOTAL PRODUCTION, THOUSANDS OF NET TONS
3.	CARBON BLACK	PRODUCTION IN MILLIONS OF POUNDS
4.	PETROLEUM	PRODUCTION OF CRUDE PETROLEUM, MILLIONS OF BARRELS
5.	PETROLEUM, ASPHALT	PRODUCTION OF ASPHALT (FROM PETROLEUM), THOUSANDS OF SHORT TONS
6.	COAL TAR	PRODUCTION, THOUSANDS OF GALLONS
7.	ISOPROPANOL	PRODUCTION, THOUSANDS OF POUNDS
8.	ASBESTOS	APPARENT CONSUMPTION, THOUSANDS OF SHORT TONS, (M.YRBK-1939)
9.	ARSENIC	PRODUCTION AND IMPORTS, THOUSANDS OF SHORT TONS
10.	CHROMITE	TOTAL SUPPLY, THOUSANDS OF TONS

SOURCE - MINERALS YEARBOOK, 1945



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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

habit and therefore cannot be attributed to it (Hueper,1926),it is unlikely that the marked variations in the onset of the rise in lung cancers in different countries,regions and communities have such an origin,unless the introduction of cigarette smoking into different population groups followed a highly erratic pattern for which any solid evidence is lacking. Such an epidemiologic scatter pattern appears to be more plausibly explained by the local development of carcinogens producing industrial operations,of tarred roads and of automobile traffic generating carcinogens containing exhausts. products,which occurred at different periods and to differing degrees (Hueper, 1926). Figs. A, B and C

b) Progression Rates

Although the majority of the proponents of the cigarette theory have maintained that the increase in lung cancers has exhibited an increasing progression rate,especially during the last 25 years,this rate has shown distinct variations for different countries and for members of the two sexes. (table 3 It has been considerable in Finland for males in Helsinki,in provincial towns and in rural areas ,buthas been rather moderate for the same population groups between 1934 to 1958 in Norway(Korpela and Magnus),where Oslo furnished the metropolitan area. Fig.4 This phenomenon was definitely less marked for females of both countries. Davies,Walker and Best also commented on the fact that lung cancer mortality in Canada had not increased to the same extent as in certain other countries,such as England and Wales and Scotland.Grzybowski and Sutherland noted that the mortality rates in Ontario appeared to be lagging some 10 years behind those of England,although during the observation period of 1931 to 1959 each succeeding cohort experienced an appreciably higher mortality rate than the preceding one covering a 5-year period. Figure 5

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

3. Differences of National Lung Cancer Rates: Protagonists of the cigarette theory have proposed that the marked differences in lung cancer mortality rates observed among some two dozen countries are attributable mainly to national variations in the consumption of cigarettes(Wynder;Doll). While statistical data on these two items give some support to this assumption,there exist several important defections from this faith. While the average annual consumption of cigarettes in the United States was in 1939 at 1,750 cigarettes and stood in 1949 at 3,186 cigarettes,and was reported for the United Kingdom at 1,955 and 2,029 cigarettes,respectively,the lung cancer rate in England for males was in 1952 two and one third times that of the United States and stood for English females almost twice as high as for American females(Dunn;Hewitt and Brooksbank). Similarly,Canadian adults consumed in 1962 approximately 3,140 cigarettes,while their English counterparts smoked in 1963 approximately 2,790 cigarettes,the age adjusted cancer mortality rates for Canadian males dying from respiratory cancers in 1951 was 17.9 per 100,000 and that for England and Wales was 45.5(Phillips,1957). A third observation equally contrary to the cigarette theory relates to the cigarette consumption and lung cancer mortality rates of Norway and Finland,two neighboring countries with many identical characteristics(Kreyberg). The annual individual consumption of cigarettes in Norway stood in 1957 at about 1,900 cigarettes and was in Finland approximately 2,160,while the lung cancer mortality rates for males were in 1959 for Norway 10.64 and for Finland 55.6(Segi). These observations presented a serious challenge to the validity of the cigarette theory and an attempt therefore was made to provide an explanation for these statistical discrepancies which would bring them in line with the basic concept. The marked differences in the degree and distribution of carcinogenic atmospheric pollutants between England and the United States furnish a plausible reason for the observed differences in lung cancer rates. The large lumber and wood processing industries associated with with occupational lung cancer hazards may account for the high lung cancer rated in Finland(Hendrickson,Walker and Cheraskin).

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

This possibility received recently some support by the observation of cancers of the nasal cavity and sinuses in wood workers(Acheson,Hadfield and Macbeth) and by the listing of wood processing workers among the occupational groups having an excssive liability to lung cancer (Berndt). It may also be mentioned in this connection that a chemical product of wood processing,dimethyl sulphate,has shown carcinogenic or cocarcinogenic properties in rats and hamsters and has been suspected as a cause of occupational cancer of the lung (Druckrey,Preussmann,Nashed, and Ivankovic;Elzay). It has been suggested also that the common practice of the sauna bath peculiar mainly to Finland may be involved through some undetermined factor in the high incidence of lung cancer among the Finnish population. The extensive use of saws and transport equipment powered by gasoline motors in the lumber industry may also create a lung cancer hazard for some of its workers through inhalation of exhaust fumes.

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Table 5

Irregular Annual Progression Rates in Various States

State	1946	1948
Alabama	4.0	5.1
Arkansas	3.6	5.4
New Mexico	2.6	3.0
North Carolina	3.1	4.0
North Dakota	5.6	4.1
Oregon	4.1	4.4
South Carolina	3.6	3.7
Washington	5.1	4.2
Wyoming	4.9	3.9

The death rates for the year 1946 were taken from «The American Cancer Society, 1949, Cancer Death Rates for each State in the United States by Site»: those for the year 1948 were produced by the National Office of Vital Statistics (Rigdon and Kirchoff).

Table 6

Incidence of Respiratory Cancer, 1937 and 1947.
Morbidity Rates for Nine Metropolitan Centers by Sex
per 100,000 population *

Primary site and city	Male			Female			Total		
	1937	1947	Percent Increase	1937	1947	Percent Increase	1937	1947	Percent Increase
Bronchus and Lung									
Atlanta	5.0	13.4	168	1.0	5.0	400	2.9	8.9	207
New Orleans	13.1	39.1	198	2.8	4.2	50	7.6	20.8	174
Dallas	5.9	29.0	392	0.5	6.4	1.180	3.1	17.2	455
Birmingham	4.5	18.9	320	2.1	3.9	86	3.3	11.0	233
Denver	9.1	21.9	141	4.2	8.1	93	6.6	14.8	124
San Francisco	15.3	34.3	120	3.9	8.1	108	9.8	20.8	112
Chicago	13.3	29.5	122	4.3	7.0	63	8.8	18.0	105
Pittsburgh	9.7	26.1	169	4.9	5.5	12	7.3	15.6	114
Detroit	12.6	32.0	154	2.3	5.7	148	7.6	19.0	150
Larynx									
Atlanta	1.4	4.0	186	0.3	0.3	—	0.9	2.0	122
New Orleans	11.3	14.9	32	0.4	1.0	150	5.6	7.6	36
Dallas	3.2	5.3	66	1.5	0.4	73	2.3	2.7	17
Birmingham	1.4	4.0	186	0.0	1.3	—	0.7	2.6	271
Denver	2.0	4.1	105	0.0	0.0	—	0.9	2.0	122
San Francisco	4.5	8.8	96	0.2	0.8	300	2.4	4.6	92
Chicago	6.7	7.0	4	0.4	0.6	50	3.5	3.7	6
Pittsburgh	4.4	8.0	82	0.4	0.8	100	2.4	4.4	83
Detroit	3.5	6.4	83	0.4	0.3	25	2.0	3.4	70

* Biometrics Section.
National Cancer Institute.

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

TABLE 8.—*Standardized mortality ratios (SMR)* for cancer of the lung in 1948–49, for the people of each State who lived in cities having a population of 100,000 or more in 1950*

State and city	Expected deaths	SMR
Alabama	132	94
Birmingham	80	81
Mobile	29	106
Montgomery	23	124
Arizona—Phoenix	36	117
Arkansas—Little Rock	30	70
California	1,448	90†
Berkeley	36	82
Long Beach	90	86
Los Angeles	690	93
Oakland	137	85
Pasadena	44	76
Sacramento	53	74
San Diego	97	77‡
San Francisco	301	94
Colorado—Denver	138	69†
Connecticut	208	85‡
Bridgeport	54	108
Hartford	61	72‡
New Haven	56	93
Waterbury	37	59†
Delaware—Wilmington	37	126
District of Columbia	221	104
Florida	183	97
Jacksonville	53	96
Miami	89	82
Tampa	41	131‡
Georgia	109	95
Atlanta	82	88
Savannah	27	116
Illinois	1,262	99
Chicago	1,224	100
Peoria	38	71
Indiana	294	80†
Evansville	39	61‡
Fort Wayne	43	72
Gary	38	121
Indianapolis	136	83‡
South Bend	38	54†
Iowa—Des Moines	60	81
Kansas	87	95
Kansas City	39	112
Wichita	48	81
Kentucky—Louisville	109	89
Louisiana	208	122†
Baton Rouge	24	34†
New Orleans	153	137†
Shreveport	31	119
Maryland—Baltimore	279	116†
Massachusetts	561	95
Boston	277	107
Cambridge	37	111
Fall River	37	90
New Bedford	41	81
Somerville	34	90
Springfield	59	63†
Worcester	76	77‡
Michigan	677	88†
Detroit	568	91‡
Flint	48	78
Grand Rapids	61	68†
Minnesota	338	68†
Duluth	41	41†
Minneapolis	190	57†
St. Paul	107	96
Missouri	450	114†
Kansas City	157	106
St. Louis	293	118†
Nebraska—Omaha	85	106
New Jersey	409	118†
Camden	39	115
Elizabeth	37	94
Jersey City	97	147†
Newark	140	118‡
Paterson	52	100
Trenton	44	103
New York	3,254	121†
Albany	51	90
Buffalo	204	105
New York City	2,699	127†
Bronx	493	127†
Brooklyn	896	121†
Manhattan	730	141†
Queens	515	114†
Richmond	65	126‡
Rochester	131	78†
Syracuse	78	84
Utica	39	66‡
Yonkers	52	87
North Carolina—Charlotte	28	32†
Ohio	973	93‡
Akron	89	71†
Canton	41	95
Cincinnati	175	97
Cleveland	306	106
Columbus	119	79‡
Dayton	75	76‡
Toledo	111	92
Youngstown	57	91
Oklahoma	120	78‡
Oklahoma City	68	75‡
Tulsa	52	82
Oregon—Portland	150	95
Pennsylvania	1,065	103
Allentown	39	70
Erie	43	79
Philadelphia	672	108‡
Pittsburgh	225	104
Reading	42	104
Scranton	44	80
Rhode Island—Providence	86	81
Tennessee	212	78†
Chattanooga	34	70
Knoxville	32	67
Memphis	98	80‡
Nashville	48	86
Texas	511	78†
Austin	31	51†
Corpus Christi	21	52‡
Dallas	113	77‡
El Paso	30	101
Fort Worth	75	61†
Houston	141	95
San Antonio	100	77‡
Utah—Salt Lake City	53	70‡
Virginia	113	125†
Norfolk	46	134‡
Richmond	67	119
Washington	292	76†
Seattle	178	84‡
Spokane	62	57†
Tacoma	52	71‡
Wisconsin—Milwaukee	220	80†
All cities in U. S. with population of 100,000 and over	14,438	100

*See text for definition and method of computing SMR.

†P=0.014 or less. (P=Probability that an equal or greater difference between state or city rate and the United States average, could arise from sampling errors.)

‡P=0.015–0.054.

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Cited from Gilliam

https://www.industrydocuments.ucsf.edu/docs/kzyk0000

in Finland(Hendrickson,Walker and Chapnerkar).

Length of Cigarette Butt: The artifice which was used for the purposes of explaining the paradoxical discrepancies between American and English rates were observations that English smokers usually smoke their cigarettes to a smaller butt before discarding them than American and Canadian smokers, and that the English smokers therefore may become exposed to larger amounts of carcinogenic combustion products accumulated in the smaller butts than the American-Canadian smokers,thereby sustaining a distinctly lesser degree of exposure(Doll;Doll,Bradford Hill and Parr;Hammond;Hammond and Wynder; Delarue). These conclusions were based on measurements taken of butts collected in various localities of the respective countries as well as in the Netherlands,using in part butts picked up from ashtrays in restaurants and other public places. In view of these obvious methodological vagaries Hammond commented on this procedure that the hoped that the method was sufficiently reliable to reveal a large difference in the average length of cigarette butts between Great Britain and the United States,and thus was justifying the conclusions drawn. Delarue went even somewhat further by suggesting that the socioeconomic differences in lung cancer rates reported from the United States by Cohart might be explained on this basis,since members of the well-to-do classes would tend to smoke cigarettes to a longer butt than members of the socioeconomic lower classes.

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The fundamental unreliability of such statistical manipulations for supporting a tottering theory is readily apparent when contemplating the statistical evidence provided by Dorn and his associates who observed in their investigations on the lung cancer mortality rates of 10 metropolitan areas in the United States similar if not larger discrepancies which cannot be attributed to differences in the length of cigarette butts in these cities,unless the original premise of Hammond and Wynder is incorrect in regard to the uniformity of the average butt length in U.S.A. Table 6 Even more marked differences in local lung cancer rates in U.S.A. were recorded by Gilliam. Table 7

Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

IMMIGRANT RATES

Table 8
Mancuso

Lung Cancer, Males 25-64

POPULATION OF...	* DEATH RATE..	IMMIGRANTS to Cuyahoga County FROM ...	* DEATH RATE..
Cuyahoga County 1947-1951 Native White	28.75	All Foreign Countries 1947-1951	38.11
England and Wales 1950	55.48	England and Wales 1947-1951	31.75
Italy 1951	16.26	Italy 1947-1951	18.61

* per 100,000 population

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

4. Lung Cancer Rates in Immigrants: The distinct improbability that national differences in the length of cigarette butts account for national differences in lung cancer rates despite divergent rates of consumption in cigarettes is indicated by another startling statistical discovery first made by Eastdott in New Zealand and subsequently confirmed by Dean in South Africa, who noted that male immigrants from Great Britain exhibited a distinctly higher lung cancer mortality than native whites of these countries, although these indulged to at least the same degree as the immigrants in cigarette smoking. Haenszel reported similar observations on migrants from England into the U.S.A., but asserted in a second report published 2 years later (Haenszel, Loveland and Sirken), that the data from U.S.A. strongly suggested that smoking class differentials would persist among all subgroups in these countries and that thus smoking habits played a significant role by implication in accounting for such differences.

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This rather convenient explanation of a proponent of the cigarette theory is open to serious doubt when considered in the light of other findings. When Graham et al. analyzed cancer rates among patients seen at the Roswell Park Memorial Hospital, they found higher lung cancer risks among female foreign-born patients and among Polish-American men. These were apparently absent among immigrant males of other ethnic derivation. Similar observations were recorded by Staszewski and Haenszel for Polish male immigrants into the United States in 1964. Also Mancuso and Coulter, who studied cancer mortality by nativity and color among residents of Ohio, noted that in highly industrialized Cuyahoga County lung cancer mortality was higher than expected among males born in Poland, Yugoslavia, and the U.S.S.R., and relatively low among Irish and Italian males, while it was similar for male immigrants from England and Wales, but considerably lower than among the male population of this country. Mancuso and Coulter concluded that this discrepancy with observations from New Zealand indicated that in part higher lung cancer mortality rates among native born ma-

Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

les 25-64 years of age for Cuyahoga County than for New Zealand during the period 1947-51 accounted for this phenomenon. The evident complexity of such statistical data on lung cancer rates of immigrants into the U.S.A. was apparent to Haenszel and Kurihara, when trying to explain the deviations of lung cancer rates among Japan born immigrants (Issei), first generation American Japanese (Nisei), Japanese, and U.S. Whites. Setting the lung cancer rates for males and females in Japan at 100, the standard mortality ratios for Issei males was 306, for Nisseis 166, and U.S.A. whites 316. The corresponding values for females were 100; 198; 129, and 131, respectively. Haenszel et al. have no explanation for the high lung cancer rate among female Isseis, and propose a highly speculative cigarette smoking causation for the male Issei lung cancer ratios. It is astounding that the supporters of the cigarette theory have not made any efforts to ascertain not only the data of individual cigarette smoking of these American immigrants, but have also determined the socioeconomic and occupational aspects of these individuals, including the home environment.

Mancuso and Coulter have emphasied, on the other hand, the low economic status and low educational level of the immigrants with high lung cancer rates. They were living moreover in parts of the community with extensive industrial establishments, some of which having known occupational and environmental lung cancer hazards, such as iron foundries. Both, Eastbott and Dean favored the view that probably exposure to carcinogenic air pollutants sustained by the immigrants during childhood and before emigration from the homeland was responsible for the higher liability of these individuals to develop lung cancer later in life.

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

From a critical study of the environmental conditions prevailing in Iceland, a country allegedly not plagued by air pollution, where the increase in lung cancer observed during recent years has been attributed by Dungal to cigarette smoking, it appears that the pollution of the homes with soot from the peat fire burning continuously through the year in farm kitchens without chimneys has provided the actual cause of lung cancers affecting members of urban and farming populations (Blalock, Kennaway, Lewis and Urquhart; Kennaway; Dungal) with a relatively low male-female sex ratio of 3:1. The exposure conditions found especially on farms thus provided lung cancer hazards in the home similar to those encountered in Mexico.

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

The probable influence of external factors apart from cigarette smoking in bringing about such abnormal lung cancer rates among immigrants has been suggested by the observation of Steiner for female Mexican immigrants to California, particularly the Los Angeles area. The lung cancer incidence among Mexican women was as high as in men of Mexican derivation, which approached that of Caucasoid inhabitants of Los Angeles. Subsequent epidemiologic studies of this observation covering all Mexican-born women in California showed a threefold excess of lung cancer deaths compared with other women of the State (Buechley, Dunn, Linden and Breslow). These investigators suggested that some exogenous factor peculiar to Mexican-born women and possibly having its major effect prior to emigration might account for this excess. Steiner was somewhat more specific in this matter by pointing out that many of these women coming from Mexico grew up in houses with no chimneys in the kitchen where the ceiling is often blackened with soot from the cooking fire. Hurwitz had a similar explanation for the excessive incidence of lung cancer in Bantus under 35 years old, when he pointed out that Bantus inhale a great deal of smoke from childhood on generated from braziers in their huts. Such an origin of a lung cancer in a Kikuyu, 35 years old, who did not smoke cigarettes was suggested also by Wilkinson, since the lungs showed black pigments from smoke of wood fires burning in the middle of hut floors. Numerous chemical analyses of soot and fumes of burning wood used for smoking meats and fishes have demonstrated the presence of carcinogenic hydrocarbons in these products of incomplete combustion of carbonaceous matter (Hueper and Conway; Kuratsune and Hueper; Kuratsune). From a sober assessment of these epidemiologic and chemical observations it seems to be much more rational to attribute the cited observations on excessive lung cancer rates among certain types of immigrants of both sexes to an exposure to carcinogenic agents in the general, occupational and home environment sustained prior to emigration and often starting from childhood than to cigarette smoking.

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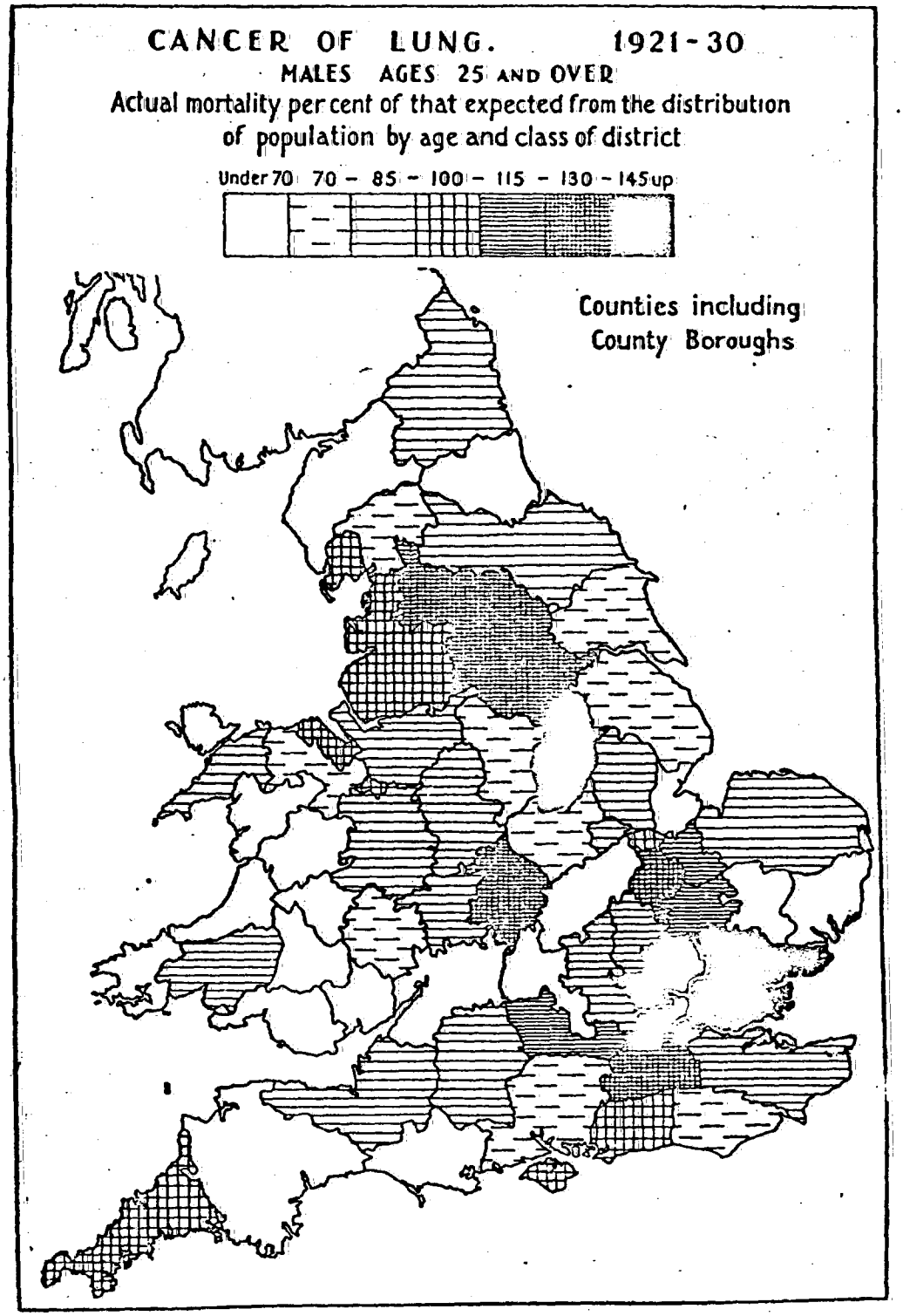
Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Figure 7



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1 Figure

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5.

Lung Cancer Rates for National Subdivisions(States,Provinces, Counties,Districts,Metropolitan Area,Communities)

The pattern of high lung cancer rates presented by highly industrialized countries is repeated when subdivisions of individual countries are analyzed for lung cancer rates in industrialized and agricultural districts. The lung cancer death rates per 100,000 population ranged in 1948 from 11.9 (New York) to 7.1(michigan),for 11 industrialized States; from 9.4(Missouri) to 7.4(Florida) for 5 regionally industrialized States; and from 5.4(Arkansas) to 3.0(new Mexico) for 9 predominantly agricultural States(Hueper,1957). A tabulation of lung cancer death rates of 1948 and rates of per capita consumption of tax-paid cigarettes revealed,on the other hand, that there was no correlation between the number of cigarettes consumed per capita and the lung cancer death rates in the different States(Rigdon and Kirchoff).

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a. States,Provinces,Counties,Districts,Prefectures: A similar distribution pattern of lung cancer deaths is presented in the map of England and Wales in which these rates are listed for the various counties(British Empire Cancer Campaign). The highest rates of 130 and up are found in the highly industrialized Midlands and in the Greater London region,while death rates of under 70 prevail in several agricultural counties. The rates express the actual mortality per cent of that expected from the distribution of population by age and class of district . The map shows pictorially also the regions in England,where the highest lung cancer mortality rates coincide with the highest rates of urban air pollution in the world. Fig. 7-10

Similar lung cancer distribution patterns are evident in the map of Belgium prepared by Firket which also reveals that the highest lung cancer rates of this country prevail in the district of Liège which is highly industrialized and affected by severe air pollution. Segi and Kurihara also noted high lung cancer rates for males and females for 5 out of 7 prefectures containing the 7 great cities and for 2 out of 4 major industrial areas(Tokyo-

Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Figure 8

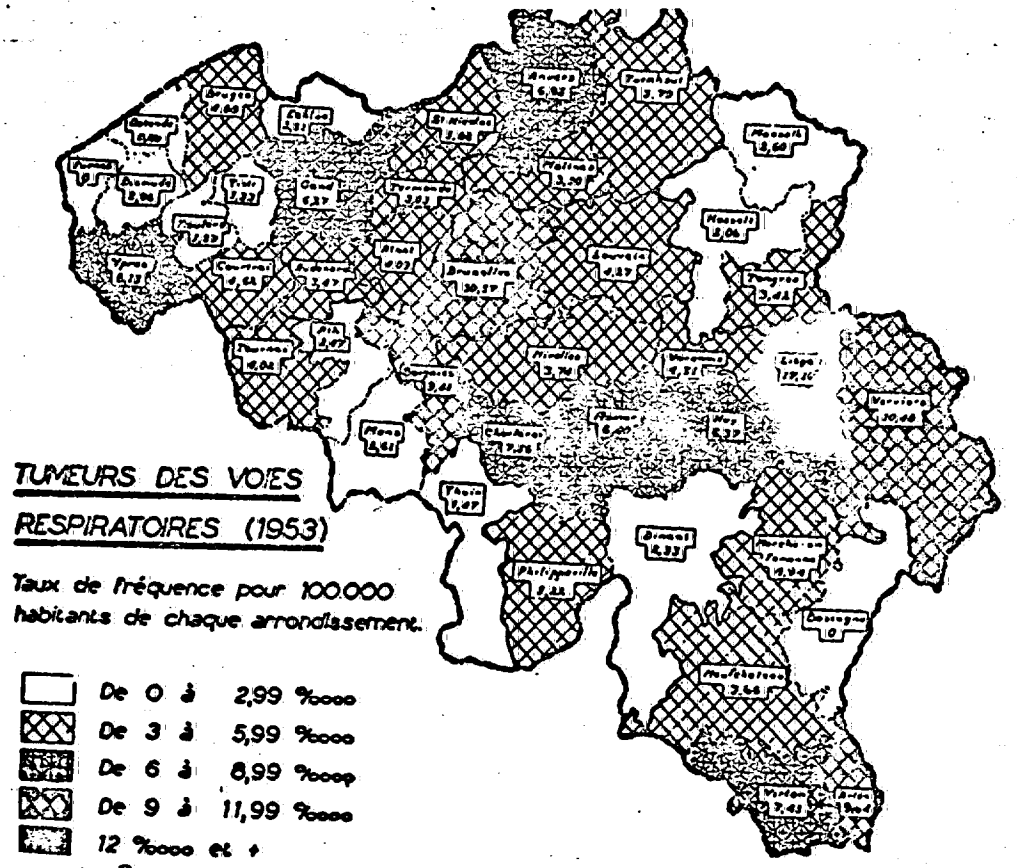

Fig. 8.—Map of Belgium giving the primary lung cancer in the different districts (reproduced from Tuyns, 1954, with permission).

Figure 9

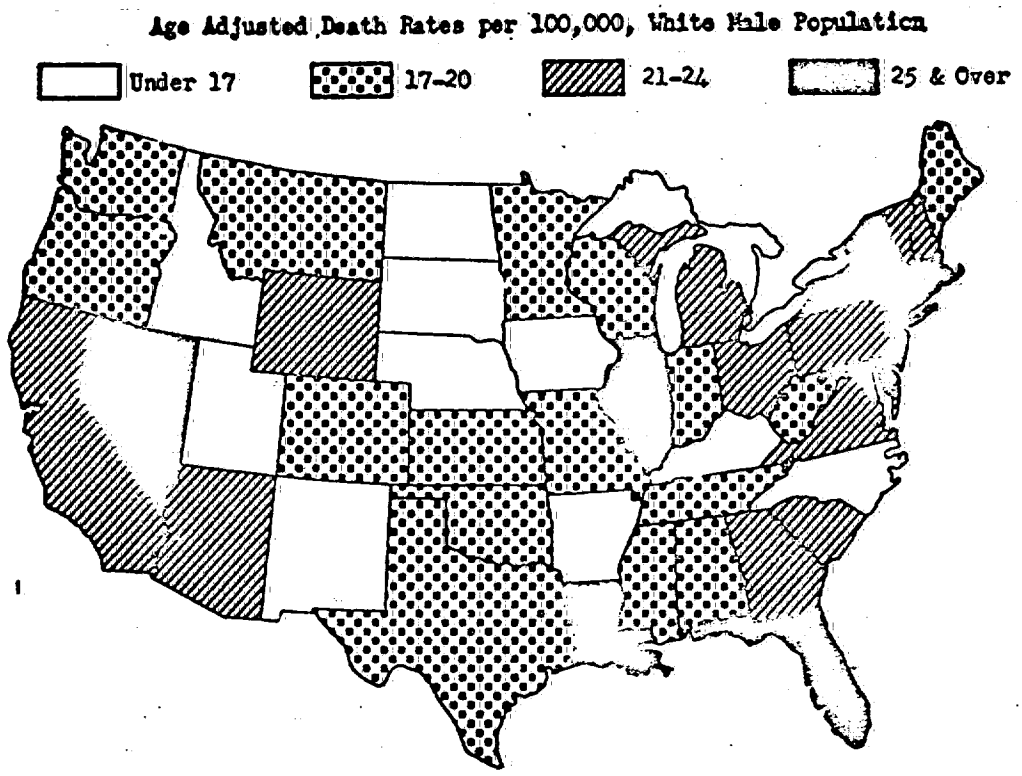

Fig. 2.—Respiratory system cancer, white males, United States, 1950. Age-adjusted death rates per 100,000 of the white male population. From Lew, E. A.: Cancer of the Respiratory Tract: Recent Trends in Mortality, *J. Internat. Coll. Surgeons* 24:12-27, 1955; published by the International College of Chicago, Chicago.

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Figure 10

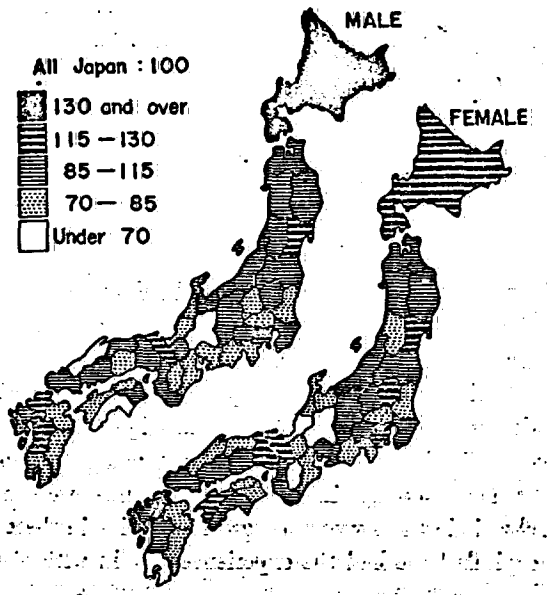

Fig. 10 Standardized mortality ratios for pulmonary cancer by prefectures, 1954–1956

(Segi and Kurihara

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Table 9

Regional Variation in Standardized Mortality Rates for Cancer of the Lungs. 1950–54. (From Registrar General 1957 p. 149.)

	Males	Females
England and Wales	100	100
NORTH OF ENGLAND	101	99
Standard regions		
Northern	87	89
East and West Ridings	98	95
North-Western	110	106
Conurbations		
Tyneside	115	116
West Yorkshire	102	92
South-East Lancashire	120	112
Merseyside	142	133
Urban areas	107	103
Rural Districts	62	70
MIDLANDS AND EASTERN ENGLAND	89	88
Standard regions		
North Midland	79	81
Midland	100	91
Eastern	86	90
Conurbation		
West Midland	119	97
Urban areas	103	97
Rural Districts	63	79
SOUTH OF ENGLAND	109	113
Standard regions		
London and South-Eastern	123	127
Southern	91	90
South-Western	78	83
Conurbation		
Greater London	127	137
Urban areas	116	117
Rural Districts	73	84
WALES (including Monmouthshire)	78	71
Wales I (South-East)	84	70
Wales II (remainder)	64	73
Urban areas	88	76
Rural Districts	59	59
URBAN AND RURAL AGGREGATES		
Urban areas	108	105
Conurbations	125	123
Areas outside conurbations	85	86
Urban areas with populations of 100,000 and over	111	100
Urban areas with populations of 50,000 and under 100,000	93	90
Urban areas with populations under 50,000	84	85
Rural Districts	66	77

cited from Case

Table 10

Lung Cancer Death Rates and Content of Air of 3.4-Benzpyrene In Communities near Liverpool
(P. Stocks)

Community	Type	Benzpyrene content in Micrograms per 100 M^3 Air	Standardized Lung Cancer Death Rate 1950-54 Expected rate 100
Conway Valley	Village	0.1	59
Llangefni	Village	0.3	53
Ruthin	Small Town	0.5	15
Blaenau	Town	0.7	62
Flint	Industrial Town	1.85	74
Ormskirk	Industrial Town	2.2	95
Hoylake	Resort City	0.3	98
Wrexham	Industrial Town	1.95	78
Chester	Industrial Town	1.45	112
Bootle	Suburb-Liverpool	3.75	146
Warrington	Industrial Town	4.4	115
St. Helens	Industrial Town	4.75	111
Birkenhead	Harbor Town	3.3	132
Liverpool	Harbor and Industrial Town	2.95-6.75	158

Table 11

MORTALITY FROM LUNG CANCER IN LONDON AND 83 COUNTY BOROUGHS AS PERCENTAGE OF NATIONAL RATE / MALES 1946-49

Bootle	194	Preston	118	Dewsbury	94
Salford	175	Newport	117	Derby	94
Liverpool	170	Warrington	116	Bath	94
Manchester	164	Stoke-on-Trent	116	Oxford	93
London	160	Wolverhampton	115	Gloucester	92
West Ham	158	Canterbury	113	Bolton	92
Smethwick	158	Grimsby	111	Portsmouth	91
Leeds	150	Bradford	111	Huddersfield	88
Wallasey	144	York	110	Wigan	88
East Ham	143	Eastbourne	109	Barnsley	83
Stockport	142	W. Bromwich	109	Ipswich	83
Brighton	141	Middlesbrough	109	Worcester	81
Kingston-on-Hull	136	Halifax	107	Rotherham	80
Birmingham	135	Bristol	103	Blackpool	80
Sheffield	135	Southampton	101	Oldham	78
Nottingham	133	Leicester	100	Merthyr-Tydfil	77
Swansea	132	Dudley	100	Bury	77
South Shields	130	Coventry	99	Barrow-in-Furness	75
St. Helens	129	Bournemouth	99	Tynemouth	74
Birkenhead	128	Hastings	99	Burton-on-Trent	74
Southend	127	Gateshead	99	Lincoln	73
Cardiff	126	Sunderland	99	Plymouth	73
Walsall	123	Doncaster	98	Exeter	72
Norwich	122	Reading	98	Burnley	69
Southport	122	Wakefield	97	West Hartlepool	66
Chester	122	Rochdale	96	Northampton	66
Newcastle-on-Tyne	121	Carlisle	95	Great Yarmouth	59
Croydon	119	Blackburn	95	Darlington	50

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Table 12

Table 12. Cancer of lung and larynx, England and Wales 1946–49 (Kennaway and Kennaway)

Type of community	Lung cancer ratio[1]		Larynx cancer ratio[1]	
	Males	Females	Males	Females
Greater London	100	100	100	100
County borough	129	137	125	55
Other urban districts	160	156	148	59
Rural districts	233	185	170	42

[1] Number of persons producing 1 death.

Table 13

TABLE 13.—*Ratio of Primary Lung Cancer Death Rates in Males Standardized for Age Distribution in 163 Metropolitan Areas to Rates for Entire United States, 1949-1951 (N. E. Manos)*

Low Ratios		High Ratios	
Green Bay, Wis.	0.2	Birmingham, Ala.	2.9
Lima, Ohio	0.3	Mobile, Ala.	2.8
Pittsfield, Mass.	0.3	Columbus, Ga.	2.5
Springfield, Mo.	0.4	Montgomery, Ala.	2.4
Wichita Falls, Texas	0.5	Durham, N. C.	2.2
Madison, Wis.	0.5	Winston-Salem, N. C.	2.1
Brockton, Mass.	0.5	Kansas City, Mo.	2.1
Utica-Rome, N. Y.	0.5	Buffalo, N. Y.	2.1
Fall River, Mass.	0.5	Columbia, S. C.	2.0
Worcester, Mass.	0.5	Rochester, N. Y.	2.0

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Yokohama and Fukuoka in Northern Kyushu). Both districts suffer from severe air pollution of mainly industrial origin. A high lung cancer death rate was found also for the northern island of Hokkaido which has coal producing centers, like Kyushu, and has a climate similar to that of England. Remarkable is the high lung cancer mortality rate in females for the Fukuoka area where large steel and chemical plants are located (130 and over , the highest general rate) and where a constant severe air pollution prevails for the area around Yahata.

The outstanding general denominator which seems to determine this distribution pattern of lung cancers is evidently industrial air-pollution.

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b. Metropolitan Areas, Cities, Towns

Death rates from lung cancer for urban communities have exhibited marked variations in several countries. According to Stocks, they have highly been correlated for large towns of England and Wales with the amounts of atmospheric deposit and smoke . This correlation has remained after allowing for differences in population density which also exhibited an association to lung cancer as has cigarette smoking. In Liverpool and North Wales region the concentration of benzpyrene and other carcinogenic hydrocarbons in the air agreed tolerably well with lung cancer death rates in districts surrounding the point of measurement (Stock and Campbell). Saruta, Yamaguchi, Ishinishi, Tsutsuni and Kodama reported that the lung cancer rate in Yahata City which has a mean amount of 3,4-benzpyrene of 16.7 gamma in 1 cbm of air was 4.1 fold that of Fukuoka City which is a commercial city without industrial air pollution and atmospherically similar to an adjacent community to Yahata City and which has a mean 3,4-benzpyrene content of 2.5 gamma per cbm. of air. Table 9-13

Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Similar epidemiologic variations were found for various American cities(Dorn et al.),in which morbidity rates of lung cancer were obtained in 1937 and 1947. The lowest rate was present for Atlanta with 13.7 per 100,000, while the highest was recorded for New Orleans (a commercial city with heavy industry in environment) with 39.1,for males. Even wider differences in urban lung cancer rates were reported by Manos in his study of primary lung cancer death ratios for males standardized for age distribution in 163 Metropolitan areas to rates for entire United States,1949-1951. The lowest ration was listed for Green Bay,Wisconsin with 0.2 and the highest one for Birmingham,Alabama with 2.9. It is most unlikely that such differences in lung cancer rates can be attributed rationally to differences in cigarette smoking habits of their respective populations of these communities,but must be due to other environmental factors. The chemical analytical data obtained by Sawicki et al. on the polynuclear aromatic hydrocarbon composition of the atmosphere in some large American cities ,however,provides a clue on the underlying causes of such differences,since distinct variations in the content of these chemicals were found in the air of the cities studied. There were not only fluctuations in the relative amounts of the various aromatic hydrocarbons which in part are known carcinogens for different communities,but also for different seasons and for their location in sunny parts of the country(west and south),where they were relatively low,and in northern or eastern less sunny parts. Intense sunlight apparently causes a photooxidative destruction of carcinogenic aromatic air pollutants and thus reduces the carcinogenic effect upon the respiratory organs of residents of communities even in the presence of severe smog. In bioassays of aromatic fractions of air pollutants obtained from Los Angeles this effect was confirmed in experimental animals by the low carcinogenic response induced in mice(Hueper et al.; Epstein).

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

While Los Angeles smog seems to be less carcinogenic for these reasons than the air pollutants of Birmingham, Alabama, they nevertheless retains carcinogenic chemicals which when inhaled act upon the human respiratory organs. The allegation of Breslow that Los Angeles smog is not carcinogenic is therefore ill founded and incorrect.

These American investigations revealed the fact that in U.S.A. the relative content of the air of 3,4-benzpyrene does not provide a reliable index for the relative carcinogenicity of the air pollutants as this was reported by Stocks. This principle may be operative where coal furnishes the principal fuel, but seems to fail where petroleum is used mainly for energy production.

Recent observations indicate that not only man but also animals kept in large cities may develop lung cancers from exposure to carcinogenic air pollutants according to evidence obtained on dogs and animal inmates of zoological gardens (Snyder and Ratcliffe; Lombard; Leake), since a role of cigarette smoking could definitely be excluded.

c.

Urban Sectors

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An adequate number of chemical investigations concerning the relative 3,4-benzpyrene content of the air of different sectors of larger cities made in Belgium; U.S.S.R.; Czechoslovakia; U.S.A. have revealed the existence of distinct variations in the concentration of this carcinogen (Pemberton; Perstudt Shabad; Dikun, Shabad and Norkin; Dimitriev and Dikun; Skramovsky) which was usually high near industrial plants or railroad stations, as well as in streets used for automobile and truck traffic particularly where the traffic flow demanded much stop-and-start driving (Sullivan and Cleary; Rose and Smith; Waller, Comming and Lawther). It is etiologically significant that other investigators found that urban sectors showing such pollutions had excessive lung cancer rates when compared with that of the remaining parts of such cities

Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Table 14

Age-Adjusted Rates by Degree of Urbanization in the United States White Population, 1949-1951, per 100,000 Population

(H.E.Menos)

Primary Cancer of the Respiratory System	Central City	Non-central City Counties	Non-metropolitan Counties
Males	11.5	9.0	5.8
Females	1.6	1.3	1.2

Figure 11

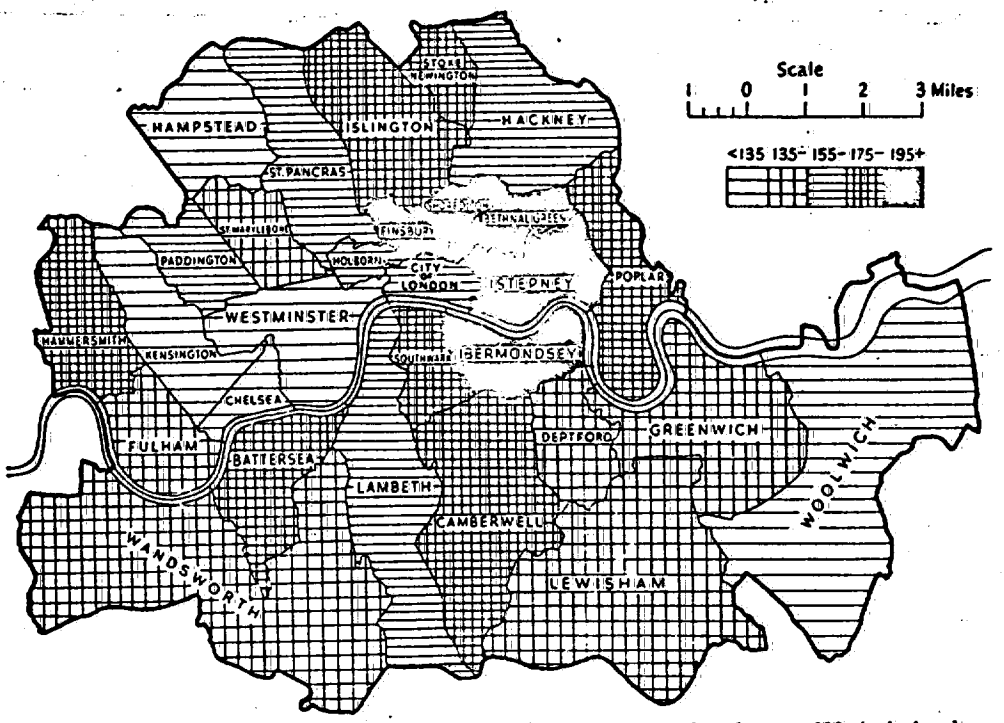

Fig. 5.—Cancer of lung, bronchus, pleura: 1946-1949 deaths of males per 100 (calculated by applying rates for England and Wales to populations at ages 0, 35, 45, 55, 65, 75+) in the City of London and Metropolitan boroughs (P. Stocks).

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000

Figure 12

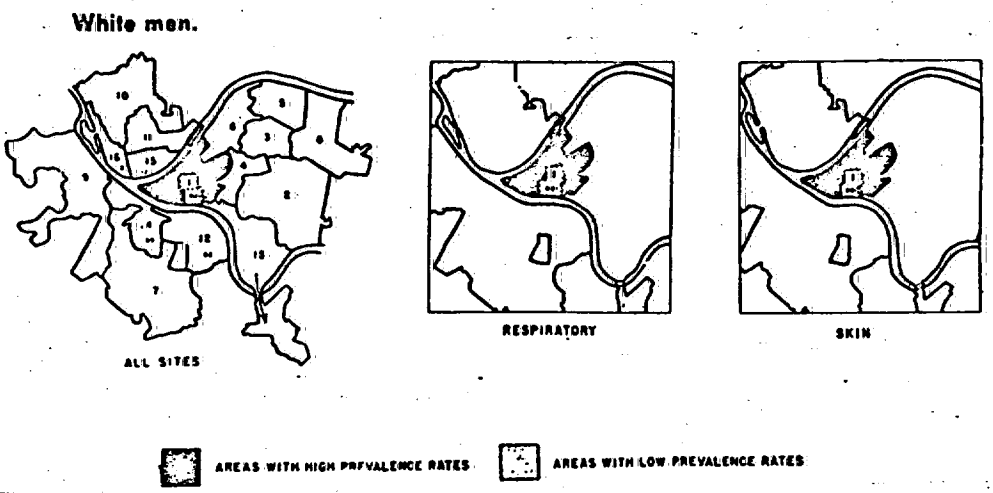

Fig. 16.—Prevalence of cancer among white men and women by site, in 16 areas of Pittsburgh, 1947 (Patno).

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Source: https://www.industrydocuments.ucsf.edu/docs/kzyk0000